

WHAT IS CLAIMED IS:

1. A method of identifying a candidate p21 pathway modulating agent, said method comprising the steps of:

- 5 (a) providing an assay system comprising a ROR polypeptide or nucleic acid;
 (b) contacting the assay system with a test agent under conditions whereby, but for the presence of the test agent, the system provides a reference activity; and
 (c) detecting a test agent-biased activity of the assay system, wherein a difference between the test agent-biased activity and the reference activity identifies the test agent as
10 a candidate p21 pathway modulating agent.

2. The method of Claim 1 wherein the assay system comprises cultured cells that express the ROR polypeptide.

- 15 3. The method of Claim 2 wherein the cultured cells additionally have defective p21 function.

4. The method of Claim 1 wherein the assay system includes a screening assay comprising a ROR polypeptide, and the candidate test agent is a small molecule
20 modulator.

5. The method of Claim 4 wherein the assay is a binding assay.

6. The method of Claim 1 wherein the assay system is selected from the group consisting
25 of an apoptosis assay system, a cell proliferation assay system, an angiogenesis assay system, and a hypoxic induction assay system.

7. The method of Claim 1 wherein the assay system includes a binding assay comprising a ROR polypeptide and the candidate test agent is an antibody.
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8. The method of Claim 1 wherein the assay system includes an expression assay comprising a ROR nucleic acid and the candidate test agent is a nucleic acid modulator.

9. The method of Claim 8 wherein the nucleic acid modulator is an antisense oligomer.

10. The method of Claim 8 wherein the nucleic acid modulator is a PMO.

11. The method of Claim 1 additionally comprising:

(d) administering the candidate p21 pathway modulating agent identified in (c) to a
5 model system comprising cells defective in p21 function and, detecting a phenotypic
change in the model system that indicates that the p21 function is restored.

12. The method of Claim 11 wherein the model system is a mouse model with defective
p21 function.

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13. A method for modulating a p21 pathway of a cell comprising contacting a cell
defective in p21 function with a candidate modulator that specifically binds to a ROR
polypeptide, whereby p21 function is restored.

15 14. The method of Claim 13 wherein the candidate modulator is administered to a
vertebrate animal predetermined to have a disease or disorder resulting from a defect in
p21 function.

15. The method of Claim 13 wherein the candidate modulator is selected from the group
20 consisting of an antibody and a small molecule.

16. The method of Claim 1, comprising the additional steps of:

(e) providing a secondary assay system comprising cultured cells or a non-human
animal expressing ROR ,

25 (f) contacting the secondary assay system with the test agent of (b) or an agent
derived therefrom under conditions whereby, but for the presence of the test agent or agent
derived therefrom, the system provides a reference activity; and

(g) detecting an agent-biased activity of the second assay system,

wherein a difference between the agent-biased activity and the reference activity of
30 the second assay system confirms the test agent or agent derived therefrom as a candidate
p21 pathway modulating agent,

and wherein the second assay detects an agent-biased change in the p21 pathway.

17. The method of Claim 16 wherein the secondary assay system comprises cultured cells.

5 18. The method of Claim 16 wherein the secondary assay system comprises a non-human animal.

19. The method of Claim 18 wherein the non-human animal mis-expresses a p21 pathway gene.

10 20. A method of modulating p21 pathway in a mammalian cell comprising contacting the cell with an agent that specifically binds a ROR polypeptide or nucleic acid.

21. The method of Claim 20 wherein the agent is administered to a mammalian animal predetermined to have a pathology associated with the p21 pathway.

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22. The method of Claim 20 wherein the agent is a small molecule modulator, a nucleic acid modulator, or an antibody.

23. A method for diagnosing a disease in a patient comprising:

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- (a) obtaining a biological sample from the patient;
- (b) contacting the sample with a probe for ROR expression;
- (c) comparing results from step (b) with a control;
- (d) determining whether step (c) indicates a likelihood of disease.

25 24. The method of Claim 23 wherein said disease is cancer.

25. The method according to Claim 24, wherein said cancer is a cancer as shown in Table 1 as having >25% expression level.

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